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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
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10/588,186

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Laurence Hermitte

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YOUNG & THOMPSON
209 Madison Street
Suite 500
ALEXANDRIA, VA 22314

EXAMINER

BROWE, DAVID

ART UNIT

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4131

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DELIVERY MODE

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PAPER

Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Office Action Summary	Application No. 10/588,186	Applicant(s) HERMITTE ET AL.	
	Examiner DAVID M. BROWE	Art Unit 4131	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

- 1) ☒ Responsive to communication(s) filed on 02 August 2006.
- 2a) ☐ This action is **FINAL**. 2b) ☒ This action is non-final.
- 3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

- 4) ☒ Claim(s) 1-20 is/are pending in the application.
- 4a) Of the above claim(s) _____ is/are withdrawn from consideration.
- 5) ☐ Claim(s) _____ is/are allowed.
- 6) ☒ Claim(s) 1-20 is/are rejected.
- 7) ☒ Claim(s) 7, 8 and 17 is/are objected to.
- 8) ☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

- 9) ☒ The specification is objected to by the Examiner.
- 10) ☐ The drawing(s) filed on _____ is/are: a) ☐ accepted or b) ☐ objected to by the Examiner.
Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).
Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).
- 11) ☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

- 12) ☒ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
- a) ☒ All b) ☐ Some * c) ☐ None of:
1. ☐ Certified copies of the priority documents have been received.
 2. ☐ Certified copies of the priority documents have been received in Application No. _____.
 3. ☒ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

- | | |
|--|---|
| 1) <input checked="" type="checkbox"/> Notice of References Cited (PTO-892) | 4) <input type="checkbox"/> Interview Summary (PTO-413) |
| 2) <input type="checkbox"/> Notice of Draftsperson's Patent Drawing Review (PTO-948) | Paper No(s)/Mail Date. _____ |
| 3) <input checked="" type="checkbox"/> Information Disclosure Statement(s) (PTO/SB/08) | 5) <input type="checkbox"/> Notice of Informal Patent Application |
| Paper No(s)/Mail Date <u>08/02/06</u> . | 6) <input type="checkbox"/> Other: _____ |

DETAILED ACTION

Specification

I. Trademarks

The use of multiple trademarks has been noted in this application. They should be capitalized wherever they appear and be accompanied by the generic terminology.

Although the use of trademarks is permissible in patent applications, the proprietary nature of the marks should be respected and every effort made to prevent their use in any manner which might adversely affect their validity as trademarks.

II. Minor Informalities

The disclosure is objected to because of the following informalities:

1. "Arthrotic" (Pg. 1, 4th paragraph) should be replaced by "arthritic".
2. "Remainance", which appears numerous times throughout the specification, does not appear in Merriam-Webster's English dictionary. An alternative word should be used; consider "continuance" or "persistence".
3. "Microphages" are referred to multiple times throughout the specification; its unclear from the context whether the inventors mean neutrophils or macrophages.
4. "...viscoelastic gel comprised by a matrix..." (Pg. 4, 2nd paragraph) should be changed to "...viscoelastic gel comprised of a matrix...".
5. "Chontroitine" and "carraghenin", which appear numerous times throughout the specification, are misspelled; chondroitin and carrageenan, respectively, should be used instead. Appropriate correction is required.

Claim Objections

I. Duplicate Claims

Claim 17 is objected to under 37 CFR 1.75 as being a substantial duplicate of claim 15. When two claims in an application are duplicates or else are so close in content that they both cover the same thing, despite a slight difference in wording, it is proper after allowing one claim to object to the other as being a substantial duplicate of the allowed claim. See MPEP § 706.03(k).

II. Minor Informalities

Claims 7 and 8 are objected to because of the following informalities:

“chondroitine” and “carraghenin” are misspelled; chondroitin and carrageenan, respectively, should be used instead. Appropriate correction is required.

Claim Rejections – 35 U.S.C. 102(b)

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

A person shall be entitled to a patent unless –

(b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

Claims 1-4, 6, 9-10, 12-14, and 18-20 are rejected under 35 U.S.C. 102(b) as being anticipated by Berg et al., USP 6,165,489, published Dec. 26, 2000.

Berg et al. disclose a biocompatible, heterogeneous crosslinked gel based on their discovery that mixing particulate crosslinked collagen with non-crosslinked collagen, then crosslinking the heterogeneous collagen mixture with a chemical crosslinking

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agent, results in crosslinked collagen compositions having specific properties that correlate with superior injectability, better extrudability from a small gauge syringe needle, and better persistence in vivo (Col. 2, Ins. 60-67; Col. 3, Ins. 1-2, 12-13; Col. 4, Ins. 1-5).

The collagen polymers can be of natural origin; for example, extracted and purified from a human or other mammalian source (Col. 6, Ins. 60-61), and should be in a pharmaceutically pure form such that it can be incorporated into a human body without generating any significant immune response (Col. 7, Ins. 3-5). Particulate crosslinked collagen is prepared by a crosslinking reaction, for example, using bi- or polyfunctional chemical crosslinking agents such as synthetic hydrophilic polymers (within which epoxys may be included), epoxides (within which epihalohydrins may be included), and divinylsulfone, or mixtures thereof (Col. 7, Ins. 7-15). The particulate crosslinked collagen is then supplemented with non-crosslinked collagen, preferably fibrillar collagen in aqueous suspension (Col. 7, Ins. 46-50; Col. 8, Ins. 4-5). It is common knowledge in the art that fibrillar collagens have molecular weights in excess of 500,000 Da. The particulate crosslinked collagen and non-crosslinked fibrillar collagen are mixed together in appropriate proportions (Col. 12, Ins. 12-14) and then undergo crosslinking using, for example, bi- or polyfunctional chemical crosslinking agents such as synthetic hydrophilic polymers (within which epoxys may be included), epoxides (within which epihalohydrins may be included), and divinylsulfone, or mixtures thereof. Unbound crosslinking agent can be removed from the composition prior to incorporation of the composition into the body of a patient (Col. 8, Ins. 25-27).

Berg et al. disclose that it is possible to manipulate specific physical properties of the heterogeneous crosslinked collagen gel by varying the concentrations and relative proportions of particulate crosslinked collagen, non-crosslinked fibrillar collagen, and crosslinking agent (Col. 3, Ins. 20-25), and by adjusting the temperature and pH (basic, neutral or acidic) of the materials (Col. 13, Ins. 24-30). Ultimately, these factors can affect critical properties of the gel, such as its extrudability from a small gauge needle, and its strength and persistence in vivo.

Berg et al. further disclose methods of using the injectable crosslinked collagen compositions for soft and hard tissue augmentation in a human patient (Col. 3, Ins 53-54; Col. 6, Ins. 31-34). Compositions can be tailored to suit the needs of a variety of medical or cosmetic applications, such as soft tissue augmentation in the face, or in other areas of the body, such as in urinary, anal, and esophageal sphincters (Col. 14, Ins. 25-30). Compositions can also be used in the production of formed implants such as tubular implants for use as vascular grafts or stents (Col. 14, Ins. 43-46).

Claim Rejections – 35 U.S.C. 103(a)

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

(a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negated by the manner in which the invention was made.

The factual inquiries set forth in *Graham v. John Deere Co.*, 383 U.S. 1, 148 USPQ 459 (1966), that are applied for establishing a background for determining obviousness under 35 U.S.C. 103(a) are summarized as follows:

1. Determining the scope and contents of the prior art.
2. Ascertaining the differences between the prior art and the claims at issue.
3. Resolving the level of ordinary skill in the pertinent art.
4. Considering objective evidence present in the application indicating obviousness or nonobviousness.

This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 CFR 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to consider the applicability of 35 U.S.C. 103(c) and potential 35 U.S.C. 102(e), (f) or (g) prior art under 35 U.S.C. 103(a).

Claims 5, 7-8, 11, and 15-17 are rejected under 35 U.S.C. 103(a) as being unpatentable over Berg et al., USP 6,165,489, in view of Lamberti et al., US 2003/0232198 A1, Zhao et al., US 2002/0049281 A1, and Hubbell et al., USP 6,060,582.

Berg et al. disclose a biocompatible, heterogeneous crosslinked gel made from collagen, a natural polymer normally found in the human body, in which particulate crosslinked collagen and non-crosslinked fibrillar collagen are mixed together in appropriate proportions and then undergo crosslinking. However, they do not disclose

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heterogeneous gels manufactured by such a process using other polymers of natural origin, including those not normally present in the human body, or from a combination of natural polymers comprising at least one normally found and one normally not found in the human body. Further, Berg et al. do not incorporate active ingredients in their gel, nor do they specify a particular method, such as dialysis, used to stop the crosslinking reaction.

Lamberti et al. disclose crosslinked hydrogel matrices that can be formed from high molecular weight polysaccharides, high molecular weight polypeptides, or combinations thereof (Pg. 5, sec. 0046). The high molecular weight polysaccharides include natural polymers such as hyaluronic acid, chondroitin sulfate, keratan sulfate, heparin, heparin sulfate, cellulose, alginate, xanthan, and carageenan (Pg. 5, sec. 0049). High molecular weight polypeptides include collagen, gelatin, keratin, and other proteins (Pg. 5, sec. 0050). They further specify that these each can be crosslinked to nucleic acids (Pg. 4, sec. 0042). Such matrices are stable and biocompatible and can be implanted in a human patient as a space filling scaffold in various medical applications. Zhao et al. teach a process for covalently crosslinking hyaluronic acid, a natural polymer normally found in the human body, to one or more biopolymers selected from cellulose, alginate, chitosan, dextran, and starch, which are natural polymers not normally found in the human body, (Pg. 2, secs. 0020, 0022) using crosslinking agents such as epoxys, epoxides, and divinylsulfone (Pg. 2, secs. 0027, 0028, 0029). Crosslinked hyaluronic acid/polymer derivatives may be produced into a gel with a high degree of stability in aqueous solution due at least in part to greater resistance to

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enzymatic digestion, and may be useful in human patients for soft or hard tissue augmentation, as implants or coatings for implants, meshes for tissue reinforcement, or joint lubricants (Pg. 6, sec. 0085). Thus, it would have been obvious to a person having ordinary skill in the art at the time of the present invention to use the above mentioned biopolymers of natural origin, and to combine natural polymers normally present and not present in the human body, in manufacturing heterogeneous biocompatible crosslinked gels with a reasonable expectation of success.

Incorporating dispersed active ingredients in gels, matrices, and scaffolds for use in a human patient is a well known practice accomplished using techniques that are well established in the art. For example, Zhao et al. disclose that the crosslinked hyaluronic acid/polymer gels may serve as a vehicle for therapeutically active factors that are incorporated therein by methods well known in the art, which may be delivered in any of the aforementioned applications (Pg. 6; secs. 0086, 0087). It would have been obvious to one of ordinary skill in the art at the time of the present invention to similarly incorporate active ingredients in a heterogeneous biocompatible crosslinked gel.

Dialysis is a common biochemical laboratory technique well known in the art for separating molecules in suspension or solution by molecular weights based on their different rates of diffusion through a semipermeable membrane. Hubbell et al. teach, for example, that albumin and hyaluronic acid can each be purified from their respective reaction mixtures with activated PEG in buffer solution using a 15,000 Da cutoff dialysis membrane during the preparation of photopolymerized biocompatible hydrogels (Col. 25, Ins. 41-42, 62-63). Given the fact, in the present invention, that the crosslinked

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polymer matrices would have dimensions significantly greater than the crosslinking agents used, it would have been obvious to one of ordinary skill in the art at the time of the present invention that dialysis would be an ideal method of choice for separating them to stop the crosslinking reaction as applicant has done with the above cited references before them.

Inquiries

Any inquiry concerning this communication or earlier communications from the examiner should be directed to DAVID M. BROWE whose telephone number is 571-270-1320. The examiner can normally be reached on Monday-Friday 7:30AM-5PM.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, James O. Wilson can be reached at 571-272-0661. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see <http://pair-direct.uspto.gov>. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

**/James O. Wilson/
Supervisory Patent Examiner, Art Unit 1624**

**David M. Browe
Patent Examiner, Art Unit 4131**